Office of Education Division of Intramural Research

FELLOWS NEWSLETTER

November 2016

The Fellows Newsletter is published monthly by the Office of Education, Division of Intramural Research, National Heart, Lung, and Blood Institute and distributed to NHLBI DIR members to promote the interest of DIR Fellows.

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Announcements

In This Issue.

From the Director of the Office of Education

The election is only one day away. This election process has been educational even for those of us who have participated in the US political process for some time. We hope it has been the same for our Visiting Fellows.

While there will be a new President in January, the major functions of the US Government continue no matter who is elected President, and so the Office of Education continues to plan events for our Fellows. These include the Career Development Seminar Series and the NHLBI Research Festival in the spring. We hope to see you there.

Director's Column

How long should I stay in an unhappy lab situation?

By Dr. Herbert Geller

Il trainees at NHLBI are here for one purpose: to acquire the knowledge, skills and experience that it takes to move to the next step in their career. This is primarily accomplished in the laboratory, with additional training provided through other support systems on campus, in-

cluding FAES, OITE, and the NHLBI Office of Education. Because most of ones time is spent in the laboratory, it is important that this is a place in which you enjoy being. But what if it's not?

There are actually only two possibilities: either you learn to accommodate to the situation in the lab, or you leave the lab. In the first situation, if things are marginal, it is possible to essentially barter your happiness for the gain of

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the scientific training. This is also a situation in which having a chat with the PI to discuss the reasons for your unhappiness may actually produce results: such as a change in projects or an increase in positive interactions between you and your PI. However, in situations in which there are irreconcilable issues, such as a project that seems to be going nowhere and an unresponsive PI, leaving the lab may be the only option.

Many fellows perceive that changing labs is career killing. Experience dictates exactly the opposite results. Many graduate students or postdoctoral fellows have successfully changed laboratories. In fact, two graduate students who got their Ph.D.s in my lab came to me from other laboratories in which they were not happy. One is now Chair of a Department, and the other recently joined the Extramural side of NIH after a productive aca-

demic career. Both were contemplating leaving school before they joined my lab.

Since coming to NIH, I have counseled many postdoctoral fellows who were unhappy in their current lab, and had decided to make a switch. In no case were they unable to obtain another lab position. I have also interviewed many incoming fellows for whom this was a second postdoctoral fellowship, and have seen them become incredibly successful in their new labs.

The mechanics of leaving are simpler than you might expect. Most PIs will entertain requests from current fellows for privacy in their job search, and will not contact the current PI. References can usually be obtained from previous mentors or their collaborators. For those who wish, confidential counseling is available through the Office of Education.



Christian Bradley is a new Postbaccalaureate Fellow under Dr. John Barrett in the Hematology Branch. She earned her B.S. in Biology from Howard University, where she was also a research assistant and resident assistant. She previously interned with the University of Louisville and the Roswell Park Cancer Institute. project will be studying a combination of factors that decrease the aggressiveness and recurrence of certain types of human cancers, evaluation of patient survival and biomarkers, and statistical analyses of the effects of treatments. tian's goal is to become a physician-scientist by pursuing a combined MD/PhD program. She plans to narrow her research interests for graduate study during her fellowship.

The Science Beat by Jordan Betz

Sandoval, P. C., Claxton, J. S., Lee, J. W., Saeed, F., Hoffert, J. D., & Knepper, M. A. (2016). Systems-level analysis reveals selective regulation of Aqp2 gene expression by vasopressin. Sci. Rep. 6, 34863.

The aquaporin family of proteins are transmembrane water channels that allow water molecules to move into or out of cells. Aquaporin-2 is a member of the aquaporin family that is activated by vasopressin, a hormone involved in water retention or excretion by the kidneys. Aquaporin-2 is normally sequestered in membrane-bound vesicles until vasopressin activates the trafficking of aquaporin-2 to the apical membrane surface. In addition to this short-term activation of aquaporin-2, vasopressin also exerts a longer-term regulatory effect on the amount of aquaporin-2 expressed. The long-term regulation of aquaporin-2 has implications in a number of different diseases related to regulating water balance.

A group of NHLBI researchers applied systems biology and computational techniques to determine whether vasopressin-regulated aquaporin-2 expressed in the collecting duct cells of the kidney is regulated at the transcriptional level and whether the effect is specific to aquaporin-2. They used two techniques to do this – RNA-Seq and ChIP-Seq of RNA Polymerase II. RNA-Seq provides deep sequencing of the mRNA transcripts in a cell (the "transcriptome") using reverse transcriptase to convert mRNA to cDNA and next-generation DNA sequencing methods to sequence the massive number of cDNAs. ChIP-Seq uses chromatin immunoprecipitation (via antibodies targeted to a subunit of RNA Polymerase II) and deep sequencing of DNA bound by RNA Polymerase II to determine the location of polymerase binding throughout the genome. This gives a snapshot of active transcription sites. These techniques were



Katherine Lindblad is a new Postbaccalaureate Fellow under Dr. Christopher Hourigan in the Hematology Branch. She earned her B.S. in Biochemistry and Molecular Biology from the University of Miami, where she was also an undergraduate lab assistant at University of Miami Miller School of Medicine. She was previously a data manager at EMMES Corporation. Her project involves gene expression profiling of the bone marrow immune microenvironment. Katherine plans to attend medical school or an MD/ PhD program after her fellowship to pursue her goals translational research.



applied to a cell line called "mpkCCD", a mouse kidney collecting duct cell line.

When treated with vasopressin, the mpkCCD cells showed an increase in the mRNA transcripts for a small number of genes (35 out of 3659) and widespread increase in overall RNA polymerase II binding throughout the genome. This means that, while vasopressin seems to cause a widespread increase in transcription, very few genes actually produce full length transcripts as a result of its action. Thus vasopressin is highly selective for increasing aquaporin-2 transcription, and exerts its effect by control of transcriptional elongation. For most genes, the RNA polymerase complex formed near the transcription start site, but then paused during its procession in the 3' direction (called "promotor proximal pausing"). However, for aquaporin-2 and a few other genes, there was binding at the transcription start site and throughout the length of the gene, enabling production of more complete transcripts.

The genes regulated by vasopressin were identified and categorized. They ranged from cell motility and cytoskeletal proteins to transcription factors and regulators of apoptosis. There were also several long non-coding RNAs that were differentially expressed, and these can have regulatory effects on transcription as well. The fact that multiple transcription factors were found to be affected (several of which have binding sites near the aquaporin-2 gene) points to the increased selectivity for regulation of aquaporin-2, which goes against a common assumption that a single transcription factor, Crebl, is responsible for vasopressin-regulated transcriptional changes.

Within tissues, and even within cells, signaling and regulatory mechanisms can be incredibly complex and difficult to dissect using traditional biochemical and molecular biological methods. The work by Sandoval, et al. demonstrates the power of a systems-level approach to this problem, providing a much more global view of changes in transcription initiation and regulation in response to stimulation with a hormone.

Recent Publications by NHLBI Fellows

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Hosokawa, K., Kajigaya, S., Feng, X., Desierto, M. J., Fernandez, I., Rios, O., Weinstein, B., Scheinberg, P., Townsley, D. M., & Young, N. S. (2016). A plasma microRNA signature as a biomarker for acquired aplastic anemia. Haematologica.

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Recent Publications by NHLBI Fellows



Craig Pearson is an NIH Oxford-Cambridge Predoctoral Fellow and Marshall Scholar under Dr. Herbert Geller in the Cell Biology and Physiology Center. As part of his Ph.D. program in Clinical Neuroscience with the University of Cambridge, he was based in the Cambridge Centre for Brain Repair until this fall, and is now conducting research at NIH. He will be looking at guidance cues in the optic chiasm, and investigating how glial cells and extracellular matrix proteins influence the growth and pathfinding of regenerating retinal ganglion cell axons in the optic nerve. Craig plans to attend medical school at Washington University in St. Louis, and then, after his residency, seek a position at a major university or teaching hospital. He hopes to conduct clinically-focused research—maintaining lab and clinical involvement while also potentially teaching classes at the graduate or medical school level.

ABCA1 (ATP-Binding Cassette Transporter A1) Mediates ApoA-I (Apolipoprotein A-I) and ApoA-I Mimetic Peptide Mobilization of Extracellular Cholesterol Microdomains Deposited by Macrophages. Arterioscler. Thromb. Vasc. Biol.

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Sodt, A. J., Venable, R. M., Lyman, E., & Pastor, R. W. (2016). Nonadditive Compositional Curvature Energetics of Lipid Bilayers. Phys. Rev. Lett. 117, 138104.

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Recent Publications by NHLBI Fellows

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arez, I., Liu, H., Waterman, C. M., Ramamurthi, K. S., La Riviere, P. J., & Shroff, H. (2016). Simultaneous multivficient engraftment and tolerance in a rhesus stem cell gene iew capture and fusion improves spatial resolution in wide-field and light-sheet microscopy. Optica. 3, 897-910.

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Q&A with an Investigator by Aparna Kishor

Postdoctoral Fellow Aparna Kishor interviews Dr. Justin Taraska.



r. Justin Taraska has been at NHLBI since 2010, pursuing a passion for illuminating cellular structures. His group exploits the exquisite structural details provided by electron microscopy to provide the environmental context for molecular positioning afforded by total internal reflection fluorescence (TIRF) and super-resolution fluorescence microscopy. By integrating the strengths

of the two imaging modalities, it becomes possible to understand the specific molecular interactions that underpin diverse cellular structures, from organelles to clatherin-coated pits.

"I have always been fascinated by natural forms."

Dr. Taraska explains that he "grew up in nature," exploring the habitat of the plants and animals of his childhood home in Florida. It is also tempting to consider the fact that his mother is an artist as another important early influence on his career. He went to college planning to study plants, but became increasingly interested in molecular mechanisms and microscopy. He found the answers to molecular questions more "satisfying" than he had originally expected, resulting in his graduate training with Wolfhard Almers, with whom he developed various microscopy techniques. In many ways, Dr. Taraska feels as though his arrival at his present career interests in single-molecule imaging was by a route opposite to that of many of his colleagues: instead of starting from interest in the physics of light, and progressing from there to applications in biology, he began with a love for the larger biological and environmental systems. This led him to the examination of the physical architecture of cells and molecules.

"In many ways, I am still investigating basic biology."

There are many challenges inherent to the pursuit of detailed molecular forms. One is to establish a way through which the field may draw simultaneously from strengths of the structural community as well as those of the imaging community. Such synergy is essential since full understanding of normal cellular physiology and, as an extension, pathology, will involve information of both types. This may require a new way of thinking or even a new way of training researchers. Regardless of the investigative strategy or methods, Dr. Taraska believes that his field has two central objectives. The first is to arrive at a physical understanding of cellular structure at the nanometer level. The second is to resolve the temporal dynamics of these nano-scale structures. Certainly both efforts will require new techniques as well as leveraging current expertise. There is still much to be uncovered about the interplay of molecules in essential cellular functions.

"Ask 'Am I enjoying what I'm doing now?""

Dr. Taraska reminds us that "science is a community enterprise." He emphasizes that it is always important to reach out to other researchers, both for personal satisfaction as well as for scientific enrichment and advancement. He recommends attending diverse conferences and having mentors outside of your own lab. While publishing papers is of central importance at all stages of this career path, it is also vital to enjoy the work at hand. After all, in science, real enthusiasm for the project and a spirit of discovery is key. "I try to remind myself and others not to obsess too much about the future, and enjoy what an amazing job this is every day," he advises. Dr. Taraska was most excited about the collegial environment and scientific energy he observed when he interviewed for his position at the NIH. Six years later, he has found that his initial impressions have been borne out. "I still can't believe I get paid for what I do." ■

MEET THE NEW FELLOWS



Graeme King is a new Research Fellow under Dr. Keir Neuman in the Biochemistry and Biophysics Center. He earned his Ph.D. in Physical Chemistry from the University of Bristol in the United Kingdom. Graeme was previously a postdoctoral researcher and lecturer at Vrije Universiteit Amsterdam in The Netherlands. His project is to use magnetic tweezers to understand the mechanism by which three proteins (TopoIII, RecQ and SSB) can resolve catenated (entangled) DNA. Graeme's goal is to obtain a tenure-track level position, and establish an independent academic career in single-molecule biophysics focusing on aspects of DNA topology.





Ryan O'Neill is a new Postdoctoral Fellow under Dr. Nasser Rusan in the Cell Biology and Physiology Center. He earned his Ph.D. in Biology from the University of New Brunswick, where he was a graduate researcher and teaching assistant. His project involves developing models for studying human centrosome diseases by replacing genes in Drosophila with their human orthologous genes and mutant alleles. He is also conducting basic science research on centrosomes, with an eye towards understanding how human disease mutations affect centrosome structure and function and downstream processes. Ryan's goal is to become a Professor/PI in an academic setting in Canada, and develop a research program that can obtain both basic science and health research funding.

Sarah Fritz is a new Postdoctoral Fellow under Dr. J. Robert Hogg in the Biochemistry and Biophysics Center. She earned her Ph.D. in Biomedical Sciences from The Ohio State University, where she was also a fellow. She was previously a visiting assistant professor of biology at Antioch College. Her project focuses on developing an in vitro reconstituted system to investigate the molecular mechanism of nonsensemediate mRNA decay. She is also working on two related projects about the role of RNA helicases in HIV-1 replication and the significance of host packaging proteins in HIV-1 RNA binding, virion assembly, and release. Her career goal is to become an academic tenure-track professor.



Matthew Restivo is a new Postdoctoral Fellow under Dr. Michael Hansen in the Biochemistry and Biophysics Center. He earned his Ph.D. in MR Physics from the University Medical Center Utrecht in The Netherlands. Matthew has previously worked as a contractor for the US Navy, and also collaborated with Zurich Med Tech in Switzerland. His project focuses on reducing the duration of the clinical cardiac MRI protocol. His career goal is to be developing and implementing MRI technology for immediate clinical use. He wants to be taking cutting-edge MR methods and applying them in a practical way to improve modern clinical imaging.

Career Development Series: Careers in Sales by Elizabeth Gordon

On September 29th, 2016, the Fellows Advisory Committee kicked off its second Career Development Seminar Series of the year with a discussion on careers in Sales. The panelists included:

- I.) **Dr. Rima Adler**, a Technical Sales Consultant from Miltenyi Biotec. She holds a Ph.D. in Genetics from GWU in a joint program with NIH. She provides technical support to labs doing cell separation and cell analysis research.
- 2.) **Dr. Elayne Provost**, a Biological Sales Specialist for Nikon Instruments, earned her Ph.D. from Yale University, and completed a posdoc at Johns Hopkins University. She provides both sales and support for NIH researchers interested in confocal and super-resolution systems.
- 3.) **Dr. Ragy Ragheb**, a Technical Specialist for Malvern Instruments, holds a Ph.D. in Macromolecular Science and Engineering. He provides applications-oriented support for the sales team and customers, both pre-sale and post-sale.
- 4.) **Berendia Jackson**, a Simple Western Sales Specialists with ProteinSimple, holds a B.S. in Microbiology and Physiology and a minor in Chemistry. She consults with clients to help them determine which protein analysis instruments will best suit their needs.
- 5.) Patrick Somers, an Applications Specialists II for MilliporeSigma, holds a Bachelors in

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Career Development Series: Careers in Sales by Elizabeth Gordon

Business Administration, and has sold Laboratory Water Purification Systems for the past 16 years.

6.) **Alison Wiedegreen**, a product category Specialists for Thermo Fisher, holds a B.S. in Chemistry and Biology, and is the official liaison between NIH researchers and Thermo Fisher Scientific sales teams. She has been with Thermo Fisher for 30 years.

Below are some key points from the discussion:

- Transition from lab bench to sales: In general, there is less direct interaction with co-workers. You tend to be more isolated, and may only see your manager a few times a year. You will likely not have an office, but rather work from home I-2 days a week when you are not visiting labs.
- Work/life balance: Sales offers a lot of flexibility. There is pressure to meet your quota, but the timing and pace at which you do that is up to each individual person, allowing for greater flexibility in your schedule. Some travel may be required.
- Let's talk salary: The salary for Technical Specialists is usually split evenly between salary and commission. Technical specialists do receive some bonuses, but this will also depend on the company. For account managers, salary is primarily based on commission.
- When asked how has a Ph.D. helped in sales, the panelists agreed that their Ph.D.'s have provided them with both great presentation as well as listening skills. These skills have enabled them to both promote their products better, but also help them understand the science behind their client's research, really allowing them to understand what products might work well for the client and how to troubleshoot when things are not working.
- When hiring individuals for a job in sales, many managers look for how you can be a resource/asset for other researchers, whether you can multitask, if you can communicate well with others, what organizational skills you have, how motivated you seem and some indication of your work ethic. You do not always need sales experience.
- The panelists enjoy the interaction with scientists and how diverse and stimulating a job in sales can be. There are constantly new products in the pipeline to learn about and promote to their researchers and this helps keep them upto-date on the newest trends and products in scientific research.

Please be sure to join us on Thursday, November 10th from 4:00 to 5:00PM, Bldg 50/Room 2328 for our next session about careers in regulatory affairs, and Wednesday, December 7th at the same time and place for careers in consulting!

ANNOUNCEMENTS

2016-2017 NHLBI DIR Tenure Track Seminar Series



This series draws a diverse audience from all areas of science represented in the NHLBI Intramural Research Program. Our first speaker is Dr. David Drubin, hosted by Dr. Justin Taraska.

"Harnessing actin dynamics for endocytic trafficking" Tuesday, Nov. 29, 2016 at 11 AM BLDG 50, RM 1227/1233

David Drubin, Ph.D.

Editor in Chief, Molecular Biology
of the Cell (MBoC)
Professor of Cell and Developmental Biology
Co-Chair, Department of Molecular
and Cell Biology
University of California, Berkeley

2016 NHLBI Halloween Bake-Off

Thank you to everyone who came to our Halloween Bake-Off, and congratulations to the winners: the Lee Lab with their colorful cupcakes!









ANNOUNCEMENTS

K22 Award Procedural Change

The procedure for receiving letters of recommendation from Dr. Robert Balaban for K22 Awards has recently changed. First, draft the letter of recommendation yourself, and forward the draft as a Word document to Dr. Herbert Geller. Dr. Geller will review the letter, and let you know if any changes need to be made. Once the letter has been finalized, please forward a PDF version to Lisa Bossert (lisa.bossert@nih.gov) for Dr. Balaban's signature. Lisa will return the signed PDF version to you directly.

Howard Hughes Medical Institute Hanna H. Gray Fellows Program

The Hanna H. Gray Fellows Program seeks to increase diversity in the biomedical research community by recruitment and retention of individuals from groups underrepresented in the life sciences. The Institute will select and support up to 15 Fellows in this first competition, which is now open for applications until February 17, 2017. Fellows will receive funding for their postdoctoral training, and if eligible, in their early career years as independent faculty. The program includes opportunities for career development, including mentoring and active involvement in the HHMI scientific community. You can find more information about the program here:

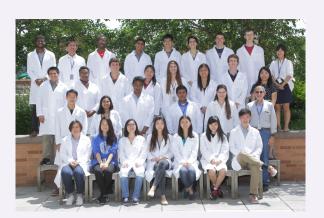
http://www.hhmi.org/programs/hanna-h-gray-fellows-program

Sarnoff Fellowship Program

The Sarnoff Fellowship Program offers medical students enrolled in accredited U.S. medical schools the opportunity to spend a year conducting intensive work in a biomedical research facility in the United States, other than the medical school in which they are enrolled. Selected fellows will receive a \$32,000 stipend, as well as allowances up to \$8000 for travel to attend the Sarnoff Annual Scientific Meeting and American Heart Association Scientific Sessions, and more. The application is open now, and the deadline for the 2017-18 Sarnoff Fellowship Program is January 11, 2017. You can find more information about the program here: https://sarnofffellowship.com/Default.asp

Summer Internship Program

Supervising a summer intern is a great way to get mentoring experience. The website for summer internship applications will open in mid-November. Please look forward to emails from the Office of Education for more policies and directions on accepting students. Thank you for making the 2016 SIP a success, and we look forward to the summer of 2017!



NHLBI Fellows Advisory Committee

FAC is always looking for new members! If you would like to represent your lab on Fellows issues, and have a say in future NHLBI events and activities, including the Annual NHLBI DIR Research Festival, please join the FAC by emailing us at: DIREDUCATION@NHLBI. NIH.GOV. Meetings are every second Monday of each month from 4 to 5PM in Building 50, Room 4229.

If you have any comments or concerns regarding your fellowship, please also feel free to contact our office.



Friday, June 9, 2017 Natcher Conference Center